(compound) which is known to have depigmenting and lightening activity when applied to the skin or hair.

Claims 1-22 stand rejected based on 35 USC 103(a) as obvious over Philippe et al WO 99/10318. This ground of rejection is respectfully traversed.

The Examiner correctly notes the disclosure in the Philippe et al disclosure that upon a possible combination of an aminophenol compound with a hydroquinone compound, it is possible to use the hydroquinone compound in lesser amounts thereby reducing the toxicity which the hydroquinone compound normally exhibits on the skin. However, in commenting about the comparative evidence provided in the specification and its effectiveness in demonstrating the superiority of the present invention over the disclosure of the reference, applicants maintain that the Examiner has not correctly assessed the evidence in light of the disclosure WO '318.

In assessing the relevancy of the '318 reference, the same must be considered in light of its disclosure without reference to any teachings of the disclosure and claims of the present application. The '318 reference describes the depigmentation and/or lightening activity of a certain group of aminophenol compounds. The only mention whatsoever of any other compound as a material which possesses skin lightening or depigmenting activity is that of kojic acid or a hydroquinone compound at page 7 of the reference, and then only in the context of a possible combination with an aminophenol compound of the reference. However, significantly, none of the Examples of the reference teach a skin lightening composition which is combination of an aminophenol compound with another compound having skin depigmenting activity. Moreover, and very importantly, Examples 1 and 3 of the reference, which describe N-ethyloxyphenol-4-aminophenol and N-cholesteryloxycarbonyl-4-aminophenol, respectively, demonstrate conclusively in the table on page 9 that N-

ethyloxyphenol-4-aminophenol is **10 times more effective** in achieving the state of depigmentation or lightening identified as Class 3 in comparison to N-cholesteryloxycarbonyl-4-aminophenol. Accordingly, applicants submit that one of skill in the art, if he were to combine a hydroquinone compound with an aminophenol compound with the expectation of obtaining a composition of some enhanced activity for skin lightening and thereby be led to reduce the amount of the hydroquinone compound in the composition to lessen toxic effects, would combine N-ethyloxyphenol-4-aminophenol with a hydroquinone compound and **not** N-cholesteryloxycarbonyl-4-aminophenol. However, the finding of the present invention which Examples 1 and 2 of the present specification demonstrate is that unexpectedly, it is not the combination of N-ethyloxyphenol-4-aminophenol with a hydroquinone compound that exhibits superior results, but rather the combination of N-cholesteryloxycarbonyl-4-aminophenol with a hydroquinone compound. Contrary to the position the Examiner takes with respect to the reliability of the data of these two examples, applicants maintain that the data of the two examples are effective in demonstrating the superiority of the present composition as claimed. N-cholesteryloxycarbonyl-4-aminophenol was taken at a lower concentration in liquid DMSO in Example 1, because, at the concentration of 6.77×10^{-5} M, the compound is at its solubility limit. On the other hand, in Example 2 , N-ethyloxyphenol-4-aminophenol is at a higher concentration of 1.25×10^{-4} M. Despite the fact that N-cholesteryloxycarbonyl-4-aminophenol is used in the lesser amount, nevertheless, in combination with the amount of hydroquinone that provides a melanogenesis inhibition of 25 %, superior activity is demonstrated for the resulting combination, this significant activity being demonstrated at an amount of N-cholesteryloxycarbonyl-4-aminophenol in the composition where the compound exhibits **no** skin lightening or depigmentation whatever when used alone! On the other hand, the data of Example 2

demonstrate that when N-ethyloxyphenol-4-aminophenol is used in a composition in an amount where the aminophenol compound alone exhibits 25 % inhibition of melanogenesis and where hydroquinone is employed at the same concentration of $8 \times {}^{-10}$ M (C_1) as in Example 1, where the compound exhibits a melanogenesis inhibition of 25 %compound; where one of skill would expect an additive effectiveness of about 50 %, in fact, the combination only exhibits 29.4 % inhibition which is well less than the sum of the effectiveness of each compound used alone! Thus, not only does the combination of Example 2 not exhibit a synergism, it is also slightly more effective than only one of the compounds of the combination alone! Clearly, the synergism exerted by the combination of the present invention is demonstrated in comparison to a most relevant combination outside the scope of the present invention, which is the combination of N-ethyloxyphenol-4-aminophenol with hydroquinone. The outstanding prior art ground of rejection is believed obviated and withdrawal of the rejection is respectfully requested.

Claims 1-23 stand rejected based on the judicially created doctrine of obviousness-type double patenting over the claims of copending U. S. application Serial No. 09/284,490.

It is pointed out that this application is the U. S. counterpart to the Philippe et al WO 99/10318 reference discussed above. As such, none of the claims describe the combination of an aminophenol compound with a hydroquinone compound. Given this fact, applicants submit that the discussion above with respect to Philippe et al is equally as relevant to the obviousness-type double patenting rejection based on the claims of the U. S. application. The fact is that none of the claims of the '490 application suggest the claimed combination of the present invention. Accordingly, withdrawal of the rejection is respectfully requested.

It is now believed that the application is in proper condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Richard L. Treanor, Ph.D.
Attorney of Record
Registration No.: 36,379

Frederick D. Vastine, Ph.D.
Registration No. 27,013

22850

TEL: 703-413-3000
FAX: 703-413-2220

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